REMARKS

Claim 21 has been amended in element (c) to correct a readily apparent typographical error. Claim 35 has been amended to include claims 20 and 21 in the claim dependency. These amendments in no way add new matter. As such, entry thereof is respectfully requested.

Restriction Requirement

The claims have been restricted into the following three groups.

Group I - Claims 19-37, drawn to a recombinant nucleic acid sequence comprising a nucleic acid of plant viral origin and designated as an IRES, sitting between two structural genes, wherein the IRES is capable of promoting expression of a 5'-distal gene from bicistronic and/or polycistronic constructs;

Group II - Claims 38 and 39, drawn to a transgenic plant transformed with a recombinant nucleic acid sequence comprising a nucleic acid sequence of plant viral origin and designated as an IRES, sitting between two structural genes, wherein the IRES is capable of promoting expression of a 5'-distal gene from bicistronic and/or polycistronic constructs in a plant cell; and

Group III - Claims 38 and 39, drawn to a transgenic animal transformed with a recombinant nucleic acid sequence comprising a nucleic acid sequence of plant viral origin and designated as an IRES, sitting between two structural genes, wherein the IRES is capable of promoting expression of a 5'-distal gene from bicistronic and/or polycistronic constructs in an animal cell.

Applicants traverse this restriction requirement and rejoinder of the claims is respectfully requested.

Eukayotic genes are monocistronic. As such, a second structure gene (coding sequence) that is located on an RNA transcript will generally not be translated in eukaryotic cells, creating a significant limitation for eukaryotic expression systems. The present inventors have overcome this limitation with the identification of internal ribosome entry sites (IRES) of plant viral origin that can be placed between a first and a second structural gene in a nucleic acid molecule (expression vector) that is to be transformed in a eukaryotic cell or organism.

As a result, all of the claims of the present invention include the feature that a first and second structural gene can be expressed simultaneously from one nucleic acid molecule in a

eukaryotic organism. All three groups identified by the Examiner have this novel common feature.

The Examiner suggests in the Restriction Requirement that the claims of the three groups have "different modes of operation, different functions or different effects" and that the claims of the three groups would require different technical consideration and search criteria. However, given the common recited basis of the invention discussed above, the claims of the three groups do not have "different modes of operation, different functions or different effects." Nor would the claims of the three groups require different technical consideration and search criteria.

All of the claims require the feature of internal ribosome entry sites (IRES) of plant viral origin that can be placed between a first and a second structural gene in a nucleic acid molecule (expression vector) that is to be transformed in a eukaryotic cell or organism. Thus, regardless of whether the host is a plant (Group II) or animal (Group III), the mode of operation, function and effects would be the same. In addition, the same technical consideration and search criteria apply, regardless of whether the transformed organism is a plant or animal. The technical consideration and search criteria are the features of the nucleic acid of the claims of Group I, i.e. an internal ribosome entry

sites (IRES) of plant viral origin that can be placed between a first and a second structural gene in a nucleic acid molecule (expression vector) that is to be transformed in a eukaryotic cell or organism. As such, the Examiner would be required to search the same feature for all of the Groups of claims. Withdrawal of the restriction requirement and rejoinder of the claims are respectfully requested.

However, in the event that the Examiner does not rejoin the claims, Applicants elect, with traverse, the claims of Group I, i.e. claims 19-37, for examination.

Election of Species

The Examiner further requires an election of species to either

a) a constitutive or

b) inducible

eukaryotic-specific promoter.

Applicants further traverse this election of species. Firstly, Applicants note that two species is not an unreasonable number of species for the Examiner to consider without requiring an election. 37 C.F.R. §1.141

In addition, the present invention does not depend on the specific type of promoter present. The promoter need only have the

property of being able to induce formation of an RNA transcript in a eukaryotic host system.

Should the Examiner choose not to withdraw the election of species, Applicants elect, with traverse, a) a constitutive promoter. In addition, the Examiner is requested to rejoin the species, b) an inducible promoter, upon the determination of the novelty and unobviousness of the generic claims.

Should the Examiner have any questions regarding the present application he is requested to please contact MaryAnne Armstrong, PhD (Reg. No. 40,069) in the Washington DC area at (703) 205-8000.

A marked-up version of claims 21 and 35 showing all changes is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fee

required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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MARKED-UP VERSION SHOWING CHANGES

Claims 21 and 35 have been amended as follows.

21. (Amended) A recombinant nucleic acid sequence comprising:

(a) a transcriptional promoter;

(b) a first structural gene expressible in eukaryotic cells linked to said transcriptional promoter;

(c) a nucleic acid sequence of plant viral origin designated as an internal ribosome entry site (IRES) by promoting cap-independent expression of a 5'-distal gene in eukaryotic cells from bicistronic and/or polycistronic mRNAs, whereby said nucleic acid sequence is ~~designated~~ **designed** by utilizing crTMV RNA sequences upstream of the MP gene or the CP gene;

(d) a second structural gene expressible in eukaryotic cells, located 3' to said IRES such that the second structural gene is placed under the translational control of said IRES, such that the first structural gene, IRES and the second structural gene are transcribed under the action of said transcriptional promoter to give a primary transcript, wherein the first structural gene of the primary transcript is able to translate by ribosome scanning mechanism and the translation of the second structural gene of the primary transcript is mediated by said IRES.

35. (Amended) A method for coexpressing two or more genes producing two or more proteins or polypeptides of interest in eukaryotic cells, comprising introducing into said cells a recombinant nucleic acid sequence according to claim 19**, 20 or 21**.